

REMARKS

The amendment to the claims is voluntary and made at the option of the assignee as being of commercial interest for immediate patent protection. Applicants intend to pursue coverage for the subject matter previously claimed in one or more separate applications.

Entry of the claim amendments does not introduce new matter into the disclosure. Support for the new claims may be found at various places in the specification, such as the following:

Claim 23:	Previous claims 12, 14, and 17; page 4 lines 34-39; Figure 4; page 15 line 33 to page 16 line 15; page 17 lines 25-39; Example 5 (pages 33-36), and throughout the disclosure
Claims 24-28	Previous claims 10 & 11; Table 3 (page 33); Table 4 (page 34)
Claim 29:	Previous claims 1 & 2
Claim 30:	Page 16 lines 27-32; page 17 lines 26-27
Claim 31:	Previous claim 18; Table 5 (page 35)
Claim 32:	Previous claim 21
Claim 33:	Previous claim 22
Claim 34:	As for claim 23; plus page 26 lines 1-28
Claims 35 & 36:	As for claim 23, plus page 26 lines 1-28; previous claim 18; Table 5 (page 35)

Applicants respectfully request examination of the application on the merits in view of these amendments.

Provisional Election of Group for Examination

It is respectfully submitted that no restriction is necessary for the claims in this application, since all the pending claims can be examined together. Claims 24-33 are method claims that depend from method claim 23, and incorporate all the limits thereof. Claim 34 claims a combination of products that are made during the practice of claim 23 when practiced on an established line of hES cells. Product claim 35 calls out the same features of the differentiated cells indicated in method claim 31. Accordingly, it would not be a burden to examine the claims together, and therefore a restriction should not be made (second paragraph of MPEP § 803).

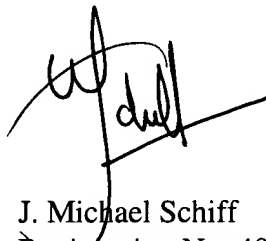
Nevertheless, in the event that the Office determines that the pending claims in this application are subject to restriction under 35 USC § 121, applicants hereby elect for examination in this application *Claim 23*, and all other claims falling in the same group.

Conclusion

No fee is believed payable for entering these amendments. The new claim set contains 14 claims; of which 3 are independent. Applicants previously paid for consideration of 22 claims in this application.

Nevertheless, should the Patent Office determine that a fee is required for further consideration of the application, the Assistant Commissioner is hereby authorized to charge such fee (or credit any overpayment) to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'J. Michael Schiff', is written over a horizontal line.

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Version with Markings to show  
**CHANGES MADE**

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Docket 090/002

***Amendment to the TITLE***

**~~DIRECT DIFFERENTIATION OF HUMAN PLURIPOTENT STEM CELLS  
AND CHARACTERIZATION OF DIFFERENTIATED CELLS~~**

**DOPAMINERGIC NEURONS OBTAINED FROM  
HUMAN EMBRYONIC STEM CELLS**

***Claim amendments***

*Cancel Claims 1-22 and substitute therefor the following:*

23. *(New)* A method for producing a neural cell population from human embryonic stem (hES) cells, comprising culturing progeny of the hES cells in a medium containing one or more added TGF- $\beta$  Superfamily Antagonists so as to produce a population in which at least 50% of the cells express either polysialylated NCAM or  $\beta$ -tubulin III.
24. *(New)* The method of claim 23, wherein the progeny are cultured in a medium containing noggin.
25. *(New)* The method of claim 23, wherein the progeny are cultured in a medium containing follistatin.
26. *(New)* The method of claim 23, wherein the medium further contains a neurotrophin.
27. *(New)* The method of claim 26, wherein the neurotrophin is NT-3 or BDNF.
28. *(New)* The method of claim 23, wherein the medium further contains a combination of factors selected from differentiation factors, neurotrophic factors, and survival factors.
29. *(New)* The method of claim 23, comprising differentiating the hES cells by plating them onto a solid surface without forming embryoid bodies or cell aggregates.
30. *(New)* The method of claim 29, wherein the solid surface comprises fibronectin or a polycation.
31. *(New)* The method of claim 23, wherein at least 10% of the MAP-2 positive cells in the produced population express tyrosine hydroxylase.
32. *(New)* The method of claim 23, further comprising combining the cell population with a compound, determining any phenotypic or metabolic changes in the cell that result from contact with the compound, and correlating the change with cellular toxicity or modulation caused by the compound.

33. (New) The method of claim 23, further comprising identifying an mRNA expressed at a different level in the neural cell population, relative to the level in undifferentiated hES cells; and preparing a polynucleotide comprising a nucleotide sequence of at least 30 consecutive nucleotides contained in the identified mRNA.
34. (New) A set of two cultured cell populations, consisting of:
  - a first cell population comprising undifferentiated cells from a line of human embryonic stem (hES) cells; and
  - a second cell population, comprising progeny of the hES cells in a medium containing one or more added TGF- $\beta$  Superfamily Antagonists.
35. (New) A set of two isolated cell populations, consisting of:
  - a first cell population comprising undifferentiated cells from a line of human embryonic stem (hES) cells; and
  - a second cell population, comprising at least ~10% hES derived neural cells, identifiable by the criteria that they are progeny of said hES cell line and express both MAP-2 and tyrosine hydroxylase.
36. (New) The set of cell populations of claim 35, wherein the second population has been produced from cells of the first population (or their progeny) by the method of claim 23.